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THE EVOLUTION OF THE CELL[1]

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WHEN addressing an audience of biologists it would be superfluous to insist upon the importance of the study of the cell and its activities. It is now recognized almost universally that the minute corpuscles known by the somewhat unsuitable term "cells" are the vital units of which the bodies of animals and plants are built up, and that all distinctive vital processes—metabolism, growth and reproduction, sexual phenomena and heredity—reduce themselves ultimately to activities taking place in, and carried on by, the individual cells which build up the body as a whole. Each cell must be regarded as a living, individual organism which, however much it may be specialized for some particular function or form of vital activity, is capable of maintaining its life and existence in a suitable environment by carrying on all the necessary processes of metabolism which are the essential and distinctive characteristics of living beings. In the case of cells composing the complex body of the higher animals and plants the cells are mutually interdependent, and, with the exception of the mature germ-cells, can not maintain their existence apart from their fellows; that is to say, the only natural[2] environment suitable for their con-

[1] Address by the President to the Zoological Section of the British Association for the Advancement of Science. Manchester, 1915.

[2] It is not necessary to do more than refer here to the investigations that have been carried on in recent years with regard to the viability and multiplication of tissue-cells removed from the body in artificial culture-media.

tinued existence is the complex body or cell-commonwealth of which they form an integral part. But in the simplest forms of life the whole body of the living individual may reach no higher degree of complexity than the single cell, which is then seen as an organism physiologically complete in every respect, living a free and independent life in Nature and competing with other organisms of all kinds, simple or complex, in the universal struggle for existence amongst living beings. This statement of the "cell-theory" is that with which, I believe, the majority of modern biologists would agree; not without, however, some dissentients, amongst whom I personally am not to be numbered.[3]

The fundamental importance of the cell as a complete living organism, whether maintaining itself singly and independently or in union with other similar but individually specialized units, has made it the object of intensive and concentrated study, not only by those who group themselves according to their special points of view as zoologists, botanists, physiologists, etc., but also by a class of investigators who take the cell itself as the subject of a branch of biological investigation termed cytology, which deals with cells in a general manner independently of their provenance, whether animal or vegetable. Some knowledge of the cell and its activities is necessary at the present time for every one concerned with the study of living things, whether that study is pursued for its own sake and with disinterested objects, or with the intention of applying scientific principles to practical aims, as in medicine or agriculture. One might have expected, therefore, that at least some elementary understanding of the nature and significance of the cell, and the importance of cellular activities in the study of life and living things, would have formed at the present time an indispensable part of the stock of knowledge acquired by all intelligent persons who are ranked as "educated" in popular esti-

These experiments afford strong support to the view that the cell is to be regarded primarily as an independent living organism.

[3] See Appendix A.

mation. Unfortunately this is so far from being the case that it is practically impossible, in this country at least, to find any one amongst the educated classes to whom the words "cell" and "cytology" convey any meaning at all, except amongst those who have interested themselves specially in some branch of biology. Consequently, any discussion concerning the cell, although it may deal with the most elementary processes of life and the fundamental activities and peculiarities of living beings, ranks in popular estimation as dealing with some abstruse and recondite subject quite remote from ordinary life and of interest only to biological specialists. It must, however, be pointed out that the general state of ignorance concerning these matters is doubtless in great part due to the fact that an objective acquaintance with cells can not be obtained without the use of expensive and delicate optical instruments.

I propose in this address to deal with an aspect of cytology which appears to me not to have received as yet the attention which it deserves, namely, the evolution of the cell itself and of its complex organization as revealed by the investigation of cytologists. Up to the present time the labors of professed cytologists have been directed almost entirely towards the study of the cell in its most perfect form as it occurs in the Metazoa and the higher plants. Many cytologists appear indeed to regard the cell, as they know it in the Metazoa and Metaphyta, as the beginning of all things, the primordial unit in the evolution of living beings.[4] For my part I would as soon postulate the special creation of man as believe that the Metazoan cell, with its elaborate organization and its extraordinarily perfected method of nuclear division by karyokinesis, represents the starting-point of the evolution

[4] For example, my friend Dr. C. E. Walker, in an article in *Science Progress* (Vol. VII, p. 639), after stating that "The unit of living matter, so far as we know, is the cell," proceeds to deal with "that form in which it is found in the multicellular and the majority of unicellular organisms, both animal and vegetable" and then describes the typical cell of the cytologist, with nucleus, cytoplasm, centrosome, chrondriosomes, and reproduction with fully developed karyokinesis.

of life. So long, however, as the attention of cytologists is confined to the study of the cells building up the bodies of the higher animals and plants, they are not brought face to face with the stages of evolution of the cell, but are confronted only with the cell as a finished and perfected product of evolution, that is to say, with cells which, although they may show infinite variation in subordinate points of structure and activity, are nevertheless so fundamentally of one type that their plan of structure and mode of reproduction by division can be described in general terms once and for all in the first chapter of a biological text-book or in the opening lecture of a course of elementary biology.

One of the most striking features of the general trend of biological investigation during the last two decades has been the attention paid to the Protista, that vast assemblage of living beings invisible, with few exceptions, to the unassisted human vision and in some cases minute beyond the range of the most powerful microscopes of to-day. The study of the Protista has received in recent years a great stimulus from the discovery of the importance of some of the parasitic forms as invaders of the bodies of men and animals and causers of diseases often of a deadly nature; it has, however, yielded at the same time results of the utmost importance for general scientific knowledge and theory. The morphological characteristic of the Protista, speaking generally, is that the body of the individual does not attain to a higher degree of organization than that of the single cell. The exploitation, if I may use the term, of the Protista, though still in its initial stages, has already shown that it is amongst these organisms that we have to seek for the forms which indicate the evolution of the cell, both those lines of descent which lead on to the cell as seen in the Metazoa and Metaphyta, as well as other lines leading in directions altogether divergent from the typical cell of the text-book. We find in the Protista every possible condition of structural differentiation and elaboration, from cells

as highly organized as those of Metazoa or even, in some cases, much more so, back to types of structure to which the term cell can only be applied by stretching its meaning to the breaking-point. Already one generalization of cytologists has been torpedoed by the study of the Protista. The dictum "Omnis nucleus e nucleo" is perfectly valid as long as it is restricted to the cells of Metazoa and Metaphyta, to the material, that is to say, to which the professed cytologist usually confines his observations.[5] But in the Protista it is now well established that nuclei can arise *de novo*, not from preexisting nuclei but from the extranuclear chromatin for which Hertwig first coined the term "chromidia."

It is clear, therefore, that the results already gained from the study of the Protista have brought about a new situation which must be faced frankly and boldly. It is impossible any longer to regard the cell as seen in the Metazoa and as defined in the text-books as the starting-point of organic evolution. It must be recognized that this type of cell has a long history of evolution behind it, which must be traced out, so far as the data permit. The construction of phylogenies and evolutionary series is of course purely speculative, since these theories relate to events which have taken place in a remote past, and which can only be inferred dimly and vaguely from such fragments of wreckage as are to be found stranded on the sands of the time in which we live. Many important stages of evolution may be totally submerged and no longer available for study and consideration. The extent to which such speculations will carry conviction to a reasonable mind will depend entirely on the stores of

[5] Vejdovský ("Zum Problem der Vererbungsträger," Prag, 1911–1912, p. 120) has already maintained, for the cells of Metazoa, that Fleming's aphorism "Omnis nucleus e nucleo" should be changed to "Omnis nucleus e chromosomatis" [*sic*], on the ground that the nucleus, as such, is not an original cell-component "but is produced secondarily from the chromosomes of the mother-cell." If this is true, there is but little difference in detail, and none in principle, between the formation of "secondary" nuclei from chromidia and the reconstruction of a daughter-nucleus from chromosomes in the most perfected form of karyokinesis.

data that can be collected and which must be the last appeal for the cogency of all arguments and judgments. The study of the Protista is as yet in its infancy; groups have been recognized and have received ponderous designations, although their very existence is yet in doubt, as in the case of the so-called Chlamydozoa; and our knowledge of the affinities and mutual relationships of the groups is still very imperfect. All attempts, therefore, to trace the evolution of the Protista must be considered as purely tentative at present. If I venture upon any such attempt, it is to be regarded as indicating a firm belief on my part that the evolution of the cell has taken place amongst the Protista, and that its stages can be traced there, rather than as a dogmatic statement that the evolution has taken place in just the manner which seems to me most probable. When we reflect on the irreconcilable differences of opinion amongst zoologists with regard to the origin and ancestry of vertebrates, for example, we may well be cautious in accepting pedigrees in Protista.

Before, however, I can proceed to deal with my main subject, it is absolutely necessary that I should define clearly the sense in which I propose to use certain terms, more especially the words "cell," "nucleus," "chromatin," "protoplasm" and "cytoplasm." Unless I do so my position is certain to be misunderstood, as, indeed, it has been already by some of my critics.

The term cell was applied originally by botanists to the single chambers or units of the honeycombed structure seen in the tissues of plants. The application of the term to such structures is perfectly natural and intelligible, since each such cell in its typical form is actually a closed space limited by firm walls, and containing a relatively large quantity of fluid cell-sap and a small quantity of the slimy protoplasmic substance. When these structures were first discovered, the limiting membrane or wall of the cell was regarded as essential, and less importance was attached to its contents. With increased knowledge,

however, and especially when animal tissues came to be studied, it became apparent that the cell-wall, like the fluid cell-sap, was a secondary product, and that the essential and primary part of the cell was the viscid protoplasmic substance, in which a peculiar body, the "nucleus," or kernel, was found to be universally present. Consequently the application and meaning of the term cell had to undergo an entire change, and it was defined as a small mass or corpuscle of the living substance, protoplasm, containing at least one nucleus. To these essential constituents other structures, such as a limiting membrane or cell-wall, and internal spaces—vacuoles—filled with watery fluid, might be added as products of the secretory or formative activity of the living substance; but such structures were no longer regarded as essential to the definition of the cell, since in many cases they are not present. It is to be regretted in some respects that with this changed point of view the term "cell," used originally under a misapprehension, was not replaced by some other term of which the ordinary significance would have been more applicable to the body denoted by it.[6]

The chief point that I wish to establish, however, is that the term cell was applied originally to the protoplasmic corpuscles building up the bodies of the Metazoa and Metaphyta, each such corpuscle consisting of a minute individualized mass of the living substance and containing a nucleus. Hence a complete cell is made up of two principal parts or regions, the nucleus and the remainder of the protoplasmic body, termed the cytoplasm. By some authors the term protoplasm is restricted to the cytoplasmic portion of the cell, and protoplasm is then contrasted with nucleus; but it is more convenient to consider the whole cell as composed of protoplasm divided into two regions, nucleus and cytoplasm.

We come now to the consideration of the body termed

[6] "Nothing could be less appropriate than to call such a body a 'cell'; yet the word has become so firmly established that every effort to replace it by a better has failed, and it probably must be accepted as part of the established nomenclature of science."—E. B. Wilson, "The Cell," p. 19.

the nucleus, which undoubtedly possesses an importance in the life and functions of the cell far greater than would be inferred from the name given to it. A nucleus, as seen in its typical form, has a limiting membrane enclosing a framework composed of a substance termed "linin." The framework has the form of a network, which is probably to be interpreted, primitively at least, as the optical expression of an alveolar structure similar to that seen also in the cytoplasm, but of coarser texture, and the apparent "threads" of the linin-framework may then be the optical sections of the partitions between neighboring alveoli. Such an interpretation does not exclude the possibility of the formation of real threads or fibers in the framework in certain cases or during particular periods of nuclear activity; just as fibrous structures may arise in the alveolar cytoplasm also. The cavities of the framework contain a watery fluid or nuclear sap, probably of the same nature as the fluid enchylema or cell-sap contained in the alveolar framework of the cytoplasm. At the nodes of the alveolar framework are lodged grains or masses of *chromatin,* a substance which must engage our most particular attention, since it is the essential constituent of the nucleus, universally present in all nuclei, whether of the simplest or of the most complex types. In addition to the chromatin-grains, which are distributed in various ways over the linin-framework, there are to be found usually one or more masses termed nucleoli, composed of a material which differs from chromatin in its reactions and has been termed plastin.

In the foregoing paragraph I have described in general terms the typical nucleus of the text-books, as found commonly in the cells that build up the bodies of ordinary animals and plants. The minutiæ of the details of structure and arrangement of the constituent parts may vary infinitely, but the type remains fairly constant. When we come, however, to the nuclei of the Protista, such pronounced modifications and variations of the type are met with that a description in general terms is no longer pos-

sible. I shall deal with some of these types later in my attempts to reconstruct the evolution and phylogeny of the cell. I will draw attention now only to a few salient points. In the Protist cell the chromatin is not necessarily confined to the nucleus, but may occur also as extranuclear grains and fragments termed chromidia, scattered through the protoplasmic body; and the chromatin may be found only in the chromidial condition, a definite nucleus being temporarily or permanently absent. Further, when a true nucleus is present in the Protist body, it seldom contains a nucleolus of the same type as that seen in the nuclei of tissue-cells, that is to say, a mass of pure plastin, but in its place is found usually a conspicuous body which shows reactions agreeing more or less closely with those of chromatin and which consists of a plastin-basis more or less densely impregnated with chromatin. Such a body is termed a karyosome (or chromatin-nucleolus) to distinguish it from the true nucleoli (plastin-nucleoli) characteristic of tissue-cells. According as the plastin or the chromatin predominates in the composition of a karyosome, its reactions may resemble more nearly those of a true nucleolus in the one case, or those of chromatin in the other. The so-called karyosomatic type of nucleus is very common in the Protista, but by no means of invariable occurrence; in many cases the nucleus consists of a clump of small grains of chromatin, with no distinct karyosome, or with a karyosome which consists mainly of plastin. Thus two extreme types of nuclear structure can be distinguished and may be termed provisionally the karyosomatic type and the granular type, ignoring for the sake of convenience in nomenclature the types of structure transitional between the two; as, for example, types in which a distinct karyosome is seen together with more or fewer peripherally arranged grains of chromatin.

In either the karyosomatic or the granular type of Protist nucleus we may find great simplification of the complex type of nuclear structure seen in the tissue-cells

of animals and plants. Thus in the first place a distinct nuclear membrane may be entirely absent and the chromatin-elements, whether occurring in the form of a compact karyosome or of a clump of grains, are lodged simply in a vacuole in the cytoplasm, that is to say in a cavity containing a watery fluid of nuclear sap in which the mass or masses of chromatin are suspended. It is a moot point, to which I shall return again, whether in nuclei of this simple type the linin-framework may sometimes be absent altogether, or whether it is invariably present in at least a rudimentary form, appearing as delicate threads (in optical section) extending from the chromatin-masses to the limiting wall of the nuclear vacuole, or between the grains of chromatin themselves. When such a framework can be detected, the nucleus acquires the appearance, in preserved preparations at least, of possessing a definite structure and is often termed a resting nucleus; many observations have shown, however, that the nucleus during life is undergoing continual internal movements and re-arrangements of its parts and is by no means at rest. The linin-framework can not, therefore, be regarded in any way as a rigid skeleton, but must be interpreted as an alveolar framework similar to that of the general protoplasm and equally liable to movement, displacement and change.

From this survey, necessarily most brief and superficial, of the manner in which the nuclei of Protists may vary from the type of nucleus described in the text-books, it is at once evident that the essential part of the nucleus is the chromatin, and that the other structural constituents of the nucleus, namely, membrane, framework, and plastin or nucleolar bodies, are to be regarded as accessory components built up round, or added to, the primary nuclear material, the chromatin. Even with regard to the nuclei of Metazoa it is maintained by Vejdovsky that at each cell-generation the entire nucleus of the daughter-cell is produced from the chromosomes alone of the

mother cell.[7] The simplest body which can be recognized as a nucleus, distinct from the chromidia scattered without order or arrangement throughout the protoplasmic body, is a mass of chromatin or a clump of chromatin-grains supported on a framework and lodged in a special vacuole in the cytoplasm. The complexity seen in the most perfect type of nucleus takes origin by progressive elaborations of, and additions to, a structure of this simple and primitive type.

This brings me to a point which I wish to emphasize most strongly, namely, that the conception of a true cell-nucleus is essentially a structural conception. A nucleus is not merely an aggregation of chromatin; it is not simply a central core of some chemical substance or material differing in nature from the remainder of the protoplasm. As Dobell has well expressed it, a pound of chromatin would not make a nucleus. The concepts "nucleus" and "chromatin" differ as do those of "table" and "wood." Although chromatin is the one universal and necessary constituent entering into the composition of the cell-nucleus, a simple mass of chromatin is not a nucleus.[8] A true nucleus is a cell-organ, of greater or less structural complexity, which has been elaborated progressively in the course of the evolution of the cell;

[7] Walker, on the other hand, considers that "it seems quite possible that the chromatin is merely a secretion of the linin." (*Science Progress*, Vol. VII, p. 641.) I doubt whether there are many cytologists who would admit this possibility, and I think that very few protistologists would assent to any such notion, since in the nuclei of Protista the linin-framework is in many cases very little in evidence, if present at all.

[8] Professor Armstrong writes: "Every organism must possess some kind of nucleus, visible or invisible: some formative center round which the various templates assemble that are active in directing the growth of the organism." (*Science Progress*, Vol. VII, p. 328.) I need hardly point out that a chemical nucleus of this kind is not in the least what the biologist or cytologist means by the term cell-nucleus. The one is a subjective postulate necessary for the comprehension of the activities of any speck of living matter or any portion, however minute, of a living organism; the other is a concrete structure, known to us by actual observation, and as much an integral part of the true cell, considered as a definite type of organism, as a backbone or its morphological equivalent is essential to the definition of a true vertebrate.

it is as much an organ of the cell as the brain is an organ of the human body. As a definite cell-organ, it performs in the life and economy of the cell definite functions, which it is the province of the cytologist to observe and to study, and if possible to elucidate and explain. As an organ of the cell, however, it has no homologue or analogue in the body of the multicellular animals or plants; there is no organ of the human body, taken as a whole, similar or comparable to the nucleus of the cell. Consequently, in studying the functions of the nucleus the human cytologist finds himself in the same difficult position that an intelligent living being lacking the sense of sight would be when trying to discover the function of visual organs in other organisms possessing that sense. There is no organ of known and understood functions with which the cytologist can compare the cell-nucleus directly.

The foregoing brief consideration of the nucleus leads me now to discuss in more detail the nature and properties of the essential nuclear substance, the so-called chromatin. To define, or characterize adequately, this substance is a difficult task. The name chromatin is derived from the fact that this substance has a peculiar affinity for certain dyes or stains, so that when a cell is treated with the appropriate coloring reagents—with so-called nuclear stains—the chromatin in the nucleus stands out sharply, by reason of being colored in a different manner from the rest of the cell. In consequence, the statement is frequently made, in a loose manner and without reflection, that chromatin is recognized by its staining reactions, but in reality this is far from being true. When a preparation of an ordinary cell is made by the methods of technique commonly in use, the chromatin is recognized and identified by its position in a definite body with characteristic structure and relations to the cell as a whole, namely the nucleus, and this is equally true whether the chromatin has been stained or not. When

the cell has been stained with one of the dyes ordinarily in use for coloring the chromatin, there are often seen in the cytoplasm grains that are colored in exactly the same manner as the chromatin-grains lodged in the nucleus. Is an extranuclear grain which stains like chromatin to be identified, *ipso facto,* as chromatin? By no means; it may or it may not be chromatin. Simple inspection of a stained preparation is altogether inadequate to determine whether such a body is or is not chromatin. Any so-called chromatin-stain colors many bodies which may occur in a cell besides the chromatin, and it may be necessary to try a great many different stains before a combination is found which will differentiate a given cytoplasmic enclosure from a true chromatin-grain by its color-reactions. The so-called volutin-grains, for example, which are found commonly in the cytoplasm of many Protists, are identified by the fact that they have a stronger affinity for "chromatin-stains" than chromatin itself.

When, moreover, chromatin is compared with regard to its staining-reactions, both in different organisms, and in the same organism at different times, it is found to react very differently to one and the same stain. A striking example of this capriciousness is seen when a preserved film is made of the blood of some vertebrate which has nucleated blood-corpuscles, such as a bird or fish, and which contains also parasitic trypanosomes. It is easy to stain the nuclei of the blood-corpuscles with various stains, as, for example, carmine-stains such as picro-carmine or alum-carmine, which will not color the nuclei of the trypanosomes in the slightest. Moreover, every cytologist knows that the "chromaticity" of the chromatin varies enormously in different phases of the nuclear cycle of generation; it is often difficult to stain the chromatin in the "resting" nucleus, but the first sign of impending nuclear division is a marked increase in the staining powers of the chromatin. There is no dye known which can be relied upon to stain chromatin always, or wherever

it occurs. Methyl-green has been claimed to be the most reliable and certain of nuclear stains, but R. Hertwig, in his classical researches upon *Actinosphærium*, showed that it sometimes fails to stain chromatin. It is perfectly conceivable that there might be varieties of chromatin which could not be stained by any dye whatsoever.

I have felt bound to insist strongly upon the inadequacy of staining-methods for the detection and identification of chromatin, well known though these facts are to every cytologist, because here also I note a tendency amongst biological chemists to regard staining-properties as the sole criterion of chromatin. In reality such properties are of entirely secondary importance. To use the terminology of formal logic, staining-properties are an "accident," though it may be an "inseparable accident," of chromatin, not a "difference" which can be used to frame a logical definition, *per genus et differentias,* of this substance. If chromatin were nothing more than "stainable substance," as Professor Armstrong terms it,[9] some of the most important results of cytological investigation would be deprived of all real significance and reduced to the merest futilities.

What then is the true criterion of the chromatin-substance of living organisms? From the chemical point of view the essential substance of the cell-nucleus would appear to be characterized by a complexity of molecular structure far exceeding that of any other proteins, as well as by certain definite peculiarities. Especially characteristic of chromatin is its richness in phosphorus-compounds, and it stands apart also from other cell-elements in its solvent reactions, for example, resistance to peptic digestion. E. B. Wilson, in his well-known treatise, has emphasized the "cardinal fact . . . that there is a definite and constant contrast between nucleus and cytoplasm." The outstanding feature of the nucleus is the constant presence in abundance of nuclein and nucleoproteins. Nuclein, which is probably identical with chromatin, is a

[9] *Science Progress,* Vol. VII, p. 327.

complex albuminoid substance rich in phosphorus. It is the phosphorus-content of chromatin that is its most characteristic chemical peculiarity as contrasted with the cytoplasm. How far these features are common, however, to all samples of chromatin in all types of living organisms universally, can not, I think, be stated definitely at present; at any rate, it is not feasible for a cytologist of these days to identify a granule in a living organism or cell as chromatin solely by its chemical reactions, although it is quite possible that at some future time purely chemical tests will be decisive upon this point—a consummation devoutly to be wished.

The only criterion of chromatin that is convincing to the present-day biologist is the test of its behavior, that is to say, its relations to the life, activity and development of the organism. I may best express my meaning by objective examples. If I make a preparation of *Arcella vulgaris* by suitable methods, I see the two conspicuous nuclei and also a ring of granules lying in the cytoplasm, stained in the same manner as the chromatin of the nuclei. Are these extranuclear granules to be regarded also as chromatin? Yes, most decidedly, because many laborious and detailed investigations have shown that from this ring of granules in *Arcella* nuclei can arise, usually termed "secondary" nuclei for no other reason than that they arise *de novo* from the extranuclear chromatin and quite independently of the "primary" nuclei. The secondary nuclei are, however, true nuclei in every respect, as shown by their structure, behavior and relations to the life-history of the organism; they may fuse as nuclei of gametes (pronuclei) in the sexual act and they become, with or without such fusion, the primary nuclei of future generations of *Arcella;* they then divide by karyokinesis when the organism reproduces itself in the ordinary way by fission, and are replaced in their turn by new secondary nuclei at certain crises in the life-history. In view of these facts it can be asserted without hesitation that the ring of staining granules in *Arcella* is composed of, or at

least contains, true chromatin-grains, extranuclear chromatin for which R. Hertwig's term chromidia is now used universally. It is interesting to note that until the life-history of *Arcella* was studied in recent times the conspicuous ring of chromidia was generally overlooked and is not shown in some of the older pictures of the organism.

If, on the other hand, I make a preparation of some unidentified amœba occurring casually in pond-water or in an infusion, and find in its cytoplasm certain grains staining in same manner as the chromatin of the nucleus, it is quite impossible, without a knowledge of the life-history of the organism, to assert definitely that the grains in question are or are not true chromidia. They might equally well turn out to be volutin or any other substance that has an affinity for the particular chromatin-stains used in making the preparation.

The fact that at the present time the only decisive criterion of what is or is not chromatin is supplied only by its behavior in the life-history and its relation to the organism, makes it much easier to identify the chromatin in some cases than in others. In those Protista or cells which contain, during the whole or a part of the life-history, one or more true nuclei, recognizable as such unmistakably by their structure and their characteristic relations to the reproductive and sexual phenomena of the organism, the chromatin can be identified with certainty. If chromidia occur in the cell-body in addition to true nuclei or even if the nuclei are temporarily absent during certain crises of the life-history and the chromatin occurs then only in the form of chromidia, there is still no difficulty in identifying the scattered chromatin-grains by the fact that they contribute, soon or later, to the formation of nuclei.

On the other hand, in the simplest Protist organisms which do not contain definite, compact nuclei recognizable by their structure and behavior, the identification of the chromatin may become correspondingly difficult. In the absence of definite chemical criteria the term chromatin

acquires then a greater or less degree of vagueness and uncertainty of application, and it is not easy to avoid a tendency to a *petitio principii* in attempting to define or identify it. To a large extent we are thrown back upon the staining-reactions, which I have already shown to be very unreliable, backed up by analogies with those forms which possess definite nuclei. Since in the cells of all animals and plants, and in all Protista which possess a true nucleus, the chromatin is the one constituent which is invariably present, as I shall point out in more detail subsequently, there is at least a strong presumption, though not of course amounting to absolute proof, that it is present, or at least is represented by some similar and genetically homologous constituents, in the forms of simpler structure also. If then in Protista of primitive type we find certain grains which exhibit the characteristic staining-reactions of chromatin to be constantly present in the organism, grains which grow and divide as a preliminary to the organism multiplying by fission and which are partitioned amongst the daughter-organisms during the process of fission, so that each daughter-individual reproduces the structure of the parent-form from which it arose; then there is very strong *prima facie* evidence, to say the least, for regarding such grains as homologous with the chromatin-grains of ordinary cells.

Having now defined or explained, as well as I am able, the terms of which I am about to make use, I return to my main theme, the cell and its evolution. To summarize the points already discussed, a typical cell is a mass of protoplasm differentiated into two principal parts or regions, the cytoplasm and the nucleus, or, it may be, two or more nuclei. The cytoplasm may or may not contain chromatin-grains in addition to other enclosures, and may possess cell-organs of various kinds. The nucleus, highly variable in minute structure, possesses one invariable constituent, the chromatin-material in the form of grains and masses of various sizes.

The cell, therefore, in its complete and typical form, is

an organism of very considerable complexity of structure and multiplicity of parts. The truth of this proposition is sufficiently obvious even from simple inspection of the structural details revealed by the microscope in cells in the so-called "resting condition," but still more so from a study of their activities and functions. The vital processes exhibited by the cell indicate a complexity of organization and a minuteness in the details of its mechanism which transcend our comprehension and baffle the human imagination, to the same extent as do the immensities of the stellar universe. If such language seems hyperbolic, it is but necessary to reflect on some of the established discoveries of cytology, such as the extraordinary degree of complication attained in the process of division of the nucleus by karyokinesis, or the bewildering series of events that take place in the nuclei of germ-cells in the processes of maturation and fertilization. Such examples of cell-activity give us, as it were, a glimpse into the workshop of life and teach us that the subtlety and intricacy of the cell-microcosm can scarcely be exaggerated.

On the assumption that an organism so complex and potent was not created suddenly, perfect and complete as it stands, but arose, like all other organisms, by progressive evolution and elaboration of some simpler form and type of structure, it is legitimate to inquire which of the various parts of the cell are the older and more primitive and which are more recent acquisitions in the course of evolution. But it must be clearly pointed out, to start with, that the problem posed in such an inquiry is perfectly distinct from, and independent of, another point which has often been discussed at length, namely, the question whether any parts of the cell, and if so which parts, are to be regarded as "living" or "active" in distinction to other parts which are to be regarded as "not-living" or "passive." This discussion, in my opinion, is a perfectly futile one, of which I intend to steer clear.

We may agree that in any given cell or living organism,

simple or complex in structure, all the parts are equally "living" and equally indispensable for the maintenance of life, or at least for the continuance of the vital functions in the normal, specific manner, without losing the right to inquire which of those parts are the phylogenetically older. A simple analogy will serve to point my meaning. A man could not continue to live for long if deprived either of his brain, his digestive tract, his lungs, his heart, or his kidneys, and each of these organs is both "living" in itself and at the same time an integral part of the entire organization of the human body; yet no one would think of forbidding comparative anatomists to discuss, from the data at their command, which of these organs appeared earlier, and which later, in the evolution of the phylum Vertebrata. Moreover, speculative though such discussions must necessarily be, there is no one possessing even a first-year student's knowledge of the facts who would controvert the statement that the digestive tract of man is phylogenetically older than the lung. Speculative conclusions are not always those that carry the least conviction.

The evolution of the cell may be discussed as a morphological problem of the same order as that of the phylogeny of any other class or phylum of living beings, and by the same methods of inquiry. In the first place there is the comparative method, whereby different types of cell-structure can be compared with one another and with organisms in which the cell-structure is imperfectly developed, in order to determine what parts are invariable and essential and what are sporadic in occurrence and of secondary importance, and if possible to arrange the various structural types in one or more evolutionary series. Secondly there is the developmental or ontogenetic method, the study of the mode and sequence of the formation of the parts of the cell as they come into existence during the life-history of the organism. Both these methods, which are founded mainly on observation, require to be checked and controlled by the experimental

methods of investigating both the functions and behavior of the organism and of its parts.

So long as cytologists limit their studies to the cells building up the tissues of the higher animals and plants, the comparative method has a correspondingly limited scope, and that of the ontogenetic method is even more restricted. Both methods receive at once, however, an enormously extended range when the Protista are taken into consideration. Then, moreover, we see the dawning possibility of another method of investigation, that, namely, of the chemical evolution of the organisms. Already some of the simpler Protista, the Bacteria, are characterized and classified largely by their chemical activities; but in more complex organisms, in those which have attained complete cell-structure, such as Protozoa, the data of chemistry do not as yet supply the evolutionist with a helpful method of investigation.

The problem of cell-evolution may be attacked by the help of the methods outlined in the foregoing remarks, beginning with the consideration of the primary structural differentiation of the typical cell, the distinction of nucleus, or rather chromatin, and cytoplasm. Since all cells known to us exhibit this differentiation, we have three possibilities as regards the manner in which it has come about, which may be summarized briefly as follows: either the cytoplasmic and chromatinic constituents of the cell have arisen as differentiations of some primitive substance, which was neither the one nor the other; or one of these two substances is a derivative of the other, in the course of evolution, either cytoplasm of chromatin, or chromatin of cytoplasm.

The idea of a primitive, undifferentiated protoplasmic substance was first put forward by Haeckel, who employed for it the term "plasson" invented by Van Beneden[10] to denote "la substance constitutive du corps des Monères et des cytodes . . . le substance formative par

[10] *Bull. de l'Acad. Roy. de Belgique*, Second Series, Vol. XXXI (1871), p. 346.

excellence.'' The simplest elementary organisms were not cells, but cytodes, ''living independent beings which consist entirely of a particle of plasson; their quite homogeneous or uniform body consists of an albuminous substance which is not yet differentiated into karyoplasm and cytoplasm, but possesses the properties of both combined.''[11] It is emphasized[12] that a sharp distinction must be drawn between protoplasm and plasson, the latter being a homogeneous albuminous formative substance (''Bildungsstoff'') corresponding to the ''Urschleim'' of the older nature-philosophy.

Haeckel, as was usual with him, did not content himself with putting forward his ideas as abstract speculations, but sought to provide them with a concrete and objective foundation by professing to have discovered, and describing in detail, living and existing organisms which were stated to remain permanently in the condition of cytodes. In consequence, a purely speculative notion was permitted to masquerade for many years under the false appearance of an objective phenomenon of nature, until the error was discovered gradually and the phantom banished from the accepted and established data of biology. Organisms supposed to be of the nature of cytodes constituted Haeckel's systematic division, Monera, of which there were supposed to be two subdivisions, the Phytomonera and the Zoomonera. The Phytomonera were stated to have the plasson colored green and to live in a plant-like manner; the Zoomonera were colorless amœboid masses of plasson which nourished themselves in the animal manner. The Bacteria were also included by Haeckel in his Monera, apparently, or at all events ranked as cytodes.[13] Most importance, however, was attributed by Haeckel to the large amœboid forms of Monera, described as without nuclei or contractile vacuoles, but as representing simply structureless

[11] *Anthropogenie,* sixth edition, Leipzig, 1910, p. 119.

[12] *Ibid.,* p. 532.

[13] *Ibid.,* p. 119.

contractile masses of albumin ("Eiweiss"), perfectly homogeneous;[14] examples of these were announced to exist under the names "Protamœba" and "Protogenes," denoting forms of life which Haeckel claimed to have discovered, but which have never been found again by any other naturalist. These organisms, as described by Haeckel, were by no means such as the modern microscopist would call minute; on the contrary, they were relatively large, and some of the forms added to the Monera by Haeckel's contemporaries might even be termed gigantic, as, for example, the supposed organism *Bathybius,* discovered in the bottles of the *Challenger* Expedition, which was believed to cover large areas of the floor of the ocean with a layer of primordial protoplasm, but which proved finally to be a precipitation by alcohol of the gypsum in sea-water.

The theory of plasson and of the cytodes of Haeckel may be considered first from the purely speculative standpoint of the origin of the living substance, a problem with which I wish to become entangled here as little as possible, since it is my object to confine myself so far as possible to deductions and conclusions that may be drawn from known facts and concrete data of observation and experiment. If, however, we postulate a chemical evolution of protoplasm, and believe that every degree of complexity exists, or at least has existed, between the simplest inorganic compounds and the immensely complicated protein-molecules of which the living substance is composed, then no doubt chemical compounds may have existed which in some sense were intermediate in their properties between the two constituents, cytoplasm and chromatin, found in all known samples of the living substance of organisms. In this sense and on such a hypothesis, a substance of the nature of plasson may perhaps be recognized or postulated at some future time by the biochemist, but this is a subject which I am quite incompetent to discuss. To the modern biologist, who can deal

[14] See his "Prinzipien der generellen Morphologie," Berlin, 1906, p. 61.

only with living things as he knows them, Haeckel's plasson must rank as a pure figment of the imagination, altogether outside the range of practical and objective biology at the present time. All visible living things known and studied up to the present consist of protoplasm, that is to say, of an extremely heterogeneous substance of complex structure, and no living organism has been discovered as yet which consists of homogeneous structureless albuminous substance. Van Beneden, who is responsible for the word plasson, though not for the cytode-theory, was under the impression that he had observed a non-nucleated homogeneous cytode-stage in the development of the gregarine of the lobster, *Gregarina (Porospora) gigantea.* Without entering into a detailed criticism of Van Beneden's observations upon this form, it is sufficient to state that the development of gregarines is now well known in all its details, and that in all phases of their life-cycle these organisms show the complete cell-structure, and are composed of nucleus and cytoplasm. Moreover, all those organisms referred by Haeckel to the group Monera which have been recognized and examined by later investigators have been found to consist of ordinary cytoplasm containing nuclei or nuclear substance (chromatin). In the present state of biological knowledge, therefore, the Monera as defined by Haeckel must be rejected and struck out of the systematic roll as a non-existent and fictitious class of organisms.

Since no concrete foundation can be found for the view that cytoplasm and chromatin have a common origin in the evolution of living things, we are brought back to the view that one of them must have preceded the other in phylogeny. The theories of evolution put forward by Haeckel and his contemporaries, if we abolish from them the notion of plasson and substitute for it that of ordinary protoplasm, would seem to favor rather the view that the earliest forms of life were composed of a substance of the nature rather of cytoplasm, and that the nuclear substance or chromatin appeared later in evolu-

tion as a product or derivative of the cytoplasm. I have myself advocated a view diametrically opposite to this, and have urged that the chromatin-substance is to be regarded as the primitive constituent of the earliest forms of living organisms, the cytoplasmic substance being a later structural complication. On this theory the earliest form of living organism was something very minute, probably such as would be termed at the present day "ultra-microscopic." After I had urged this view in the discussion on the origin of life at the Dundee Meeting of the British Association in 1912 a poem appeared in *Punch*,[15] dividing biologists into "cytoplasmists" and "chromatinists." I must confess myself still a whole-hearted chromatinist. But before I consider this point I may refer briefly to some other speculations that have been put forward with regard to the nature of the earliest form of life. It is manifestly quite impossible that I should undertake here to review exhaustively all the theories and speculations with regard to the origin of life and the first stages in its evolution that have been put forward at different times. I propose to limit myself to the criticism of certain theories of modern times which, recognizing the fundamental antithesis between chromatin and cytoplasm, regard these two cell-constituents as representing types of organisms primitively distinct, and suggest the hypothesis that true cells have arisen in the beginning as a process of symbiosis between them. Boveri, whose merits as a cytologist need no proclamation by me, was the first I believe to put forward such a notion; he enunciated the view that the chromosomes were primitively independent elementary organisms which live symbiotically with protoplasm, and that the organism known as the cell arose from a symbiosis between two kinds of simple organisms, "Monera."[16]

A similar idea lies at the base of the remarkable and

[15] Vol. CXLIII, p. 245.

[16] *Fide* Vejdovsky, *l. c.* I have not had access to the work of Boveri, in which he is stated to have put forward these ideas.

ingenious speculations of Mereschkowsky,[17] who assumes a double origin for living beings from two sorts of protoplasm, supposed not only to differ fundamentally in kind but also to have had origins historically distinct. The first type of protoplasm he terms mycoplasm,[18] which is supposed to have come into existence during what he calls the third epoch[19] of the earth's history, at a time when the crust of the earth had cooled sufficiently for water to be condensed upon it, but when the temperature of the water was near boiling-point; consequently the waters of the globe were free from oxygen, while saturated with all kinds of mineral substances. The second type of protoplasm was amœboplasm, the first origin of which is believed to have taken place during a fourth terrestrial epoch when the waters covering the globe were cooled down below 50° C., and contained dissolved oxygen but fewer mineral substances. Corresponding with the differences of the epoch and the conditions under which they arose, Mereschkowsky's two types of protoplasm are distinguished by sharp differences in their nature and constitution.

Mycoplasm, of which typical examples are seen in bacteria, in the chromatin-grains of the nucleus and the chromatophores of plant-cells, is distinguished from amœboplasm, which is simply cytoplasm, by the following points. (1) Mycoplasm can live without oxygen, and did so in the beginning at its first appearance when the temperature of the hydrosphere was too high for it to have contained dissolved oxygen; only at a later period, when the temperature became low enough for the water to contain oxygen in solution, did some of the forms begin

[17] Mereschowsky, C., "Theorie der zwei Plasmaarten als Grundlage der Symbiogenesis, einer neuen Lehre von der Entstehung der Organismen," *Biol. Centralblatt,* XXX, 1910, pp. 278–303, 321–347, 353–367.

[18] The term mycoplasm used by Mereschowsky must not be confounded with the similar word used by Eriksson and other botanists in reference to the manner in which Rust-Fungi permeate their hosts.

[19] In the first epoch the earth was an incandescent mass of vapor; in the second it had a firm crust, but the temperature was far too high to permit of the condensation of water-vapor upon its surface.

to adapt themselves to these conditions, and became secondarily facultative or obligate aerobes. Amœboplasm, on the other hand, can not exist without a supply of oxygen. (2) Mycoplasm can support temperatures of 90° C. or even higher; amœboplasm can not support a temperature higher than 45° C. or 50° C. (3) Mycoplasm is capable of building up albumins and complex organic substances from inorganic materials; amœboplasm is incapable of doing so, but requires organic food. (4) Mycoplasm has restricted powers of locomotion and is incapable of amœboid movement, or of forming the contractile vacuoles seen commonly in amœboplasm. (5) Mycoplasm, in contrast to amœboplasm, is rich in phosphorus and nuclein. (6) Mycoplasm is extraordinarily resistant to poisons and utilizes as food many substances that are extremely deadly to amœboplasm, such as prussic acid, strychnine and morphia. (7) Amongst minor differences, mycoplasm is characterized by the presence of iron in the combined state and possesses a far more complicated structure than amœboplasm, a peculiarity which enables mycoplasmic cell-elements (chromosomes) to function as the bearers of hereditary qualities.

The course of the evolution of living beings, according to Mereschkowsky, was as follows. The earliest forms of life were "Biococci," minute ultra-microscopic particles of mycoplasm, without organization, capable of existing at temperatures near boiling-point and in the absence of oxygen, possessing the power of building up proteins and carbohydrates from inorganic materials, and very resistant to strong mineral salts and acids and to various poisons. From the Biococci arose in the first place the Bacteria, which for a time were the only living inhabitants of the earth. Later, when the temperature of the terrestrial waters had been lowered below 50° C., and contained abundant organic food in the shape of Bacteria, amœboplasm made its appearance in small masses as non-nucleated Monera which crept in an amœboid manner on the floor of the ocean and devoured Bacteria.

The next step in evolution is supposed to have been that, in some cases, micrococci ingested by the Monera resisted digestion by them and were enabled to maintain a symbiotic existence in the amœboplasm. At first the symbiotic micrococci were scattered in the Moneran body, but later they became concentrated at one spot, surrounded by a membrane, and gave rise to the cell-nucleus. In this way, by a "symbiogenesis" or process of symbiosis between two distinct types of organisms, Mereschkowsky believes the nucleated cell to have arisen, an immense step forward in evolution, since the locomotor powers of the simple and delicate Monera were now supplemented by the great capability possessed by the Bacteria of producing ferments of the most varied kinds.

Meanwhile it is supposed that the free Bacteria continued their natural evolution and gave rise to the Cyanophyceæ, and to the whole group of Fungi. The plant-cell came into existence by a further process of symbiogenesis, in that some of the Cyanophyceæ, red, brown or green in color, became symbiotic in nucleated cells, for the most part flagellates, in which they established themselves as the chromatophores or chlorophyll-corpuscles. In this way Mereschkowsky believes the vegetable cell to have come into existence, and the evolution of the Vegetable Kingdom to have been started, as a double process of symbiosis. Those amœboid or flagellated organisms, on the other hand, which formed no symbiosis with Cyanophyceæ, continued to live as animals and started the evolution of the Animal Kingdom.

As a logical deduction from this theory of the evolution of living beings, Mereschkowsky classifies organisms generally into three groups or Kingdoms: first the Mycoidea, comprising Bacteria, Cyanophyceæ, and Fungi, and in which no symbiosis has taken place; secondly, the Animal Kingdom, in which true cells have arisen by a simple symbiosis of mycoplasm (chromatin) and amœboplasm (cytoplasm); thirdly, the Vegetable Kingdom, in which true

cells have entered upon an additional symbiosis with Cyanophyceæ, chromatophores or chlorophyll-corpuscles.

Interesting and suggestive as are the speculations of Mereschkowsky, they are nevertheless open to criticism from many points of view. I will not enter here into criticisms which I regard as beyond my competence. It is for botanists to pronounce upon the notion that Bacteria, Cyanophyceæ, and Fungi can be classified together as a group distinct from all other living beings; to decide whether the protoplasm of the Cyanophyceæ and Fungi can be regarded as consisting of mycoplasm alone, and not of a combination of nuclei and cytoplasm, such as is found in true cells and represents, according to Mereschkowsky, a symbiosis of mycoplasm and amœboplasm. I think I am right in saying that botanists are agreed in regarding Fungi as derived from green algæ, and as possessing nuclei similar to those of the higher plants. As a zoologist the point that strikes me most is the absence of any evidence that true Monera, organisms consisting of cytoplasm alone, exist or could ever have existed. Mereschkowsky supposes that when the Monera came into being they maintained their existence by feeding upon Bacteria. In order to digest Bacteria, however, the Monera must have been capable of producing ferments, and therefore did not acquire this power only as the result of symbiosis with Bacteria, unless it be assumed that the symbiosis came about at the instant that amœboplasm came into existence. There is, however, no evidence that cytoplasm by itself can generate ferments. All physiological experiments upon the digestion of Protozoa indicate that the cytoplasmic body, deprived of the nucleus, can not initiate the digestive process. Consequently the existence of purely cytoplasmic organisms would seem to be an impossibility.

For my part, I am unable to accept any theory of the evolution of the earliest forms of living beings which assumes the existence of forms of life composed entirely of cytoplasm without chromatin. All the results of modern

investigations into the structure, physiology and behavior of cells on the one hand, and of the various types of organisms grouped under the Protista, on the other hand—the combined results, that is to say, of cytology and protistology—appear to me to indicate that the chromatin-elements represent the primary and original living units or individuals, and that the cytoplasm represents a secondary product. I will summarize briefly the grounds that have led me to this conviction, and will attempt to justify the faith that I hold; but first I wish to discuss briefly certain preliminary considerations which seem to me of great importance in this connection.

It is common amongst biologists to speak of "living substance," this phrase being preceded by either the definite or the indefinite article—by either "the" or "a." If we pause to consider the meaning of the phrase, it is to be presumed that those who make use of it employ the term "substance" in the usual sense to denote a form of matter to which some specific chemical significance can be attached, which could conceivably be defined more or less strictly by a chemist, perhaps even reduced to a chemical formula of some type. But the addition of the adjective "living" negatives any such interpretation of the term "substance," since it is the fundamental and essential property of any living being that the material of which it is composed is in a state of continual molecular change and that its component substance or substances are inconstant in molecular constitution from moment to moment. When the body of a living organism has passed into a state of fixity of substance, it has ceased, temporarily or permanently, to behave as a living body; its fires are banked or extinguished. The phrase "living substance" savors, therefore, of a *contradictio in adjecto;* if it is "living" it can not be a "substance," and if it is a "substance" it can not be "living."

As a matter of fact, the biologist, when dealing with purely biological problems, knows nothing of a living substance or substances; he is confronted solely by living in-

dividuals, which constitute his primary conceptions, and the terms "life" and "living substance" are pure abstractions. Every living being presents itself to us as a sharply-limited individual, distinct from other individuals and constituting what may be termed briefly a microcosmic unit, inasmuch as it is a unity which is far from being uniform in substance or homogeneous in composition, but which, on the contrary, is characterized by being made up of an almost infinite multiplicity of heterogeneous and mutually interacting parts. We recognize further that these living individuals possess invariably specific characteristics; two given living individuals may be so much alike that we regard them as of the same kind or "species," or they may differ so sharply that we are forced to distinguish between them specifically. Living beings are as much characterized by this peculiarity of specific individuality as by any other property or faculty which can be stated to be an attribute of life in general, and this is true equally of the simplest or the most complex organisms; at least we know of no form of life, however simple or minute, in which the combined features of individuality and specificity are not exhibited to the fullest extent. A living organism may be so minute as to elude direct detection entirely by our senses, even when aided by all the resources furnished by modern science; such an organism will, nevertheless, exhibit specific properties or activities of an unmistakable kind, betraying its presence thereby with the utmost certainty. The organisms causing certain diseases, for example, are ultra-microscopic, that is to say, they have not been made visible as yet, and an exact description or definition can not be given of them at the present time; yet how strongly marked and easily distinguishable are the specific effects produced by the organisms causing, respectively, measles and small-pox, for instance, each, moreover, remaining strictly true and constant to its specific type of activity; the organism, whatever its nature may be, which causes measles can not

give rise to small-pox, nor *vice versa*, but each breeds as true to type as do lions and leopards.

The essential and distinctive characteristic of a living body of any kind whatsoever is that it exhibits while it lives permanence and continuity of individuality or personality, as manifested in specific behavior, combined with incessant change and lability of substance; and further, that in reproducing its kind, it transmits its specific characteristics, with, however, that tendency to variability which permits of progressive adaptation and gradual evolutionary change. It is the distinctively vital property of specific individuality combined with "stuff-change" (if I may be allowed to paraphrase a Teutonic idiom) which marks the dividing line between biochemistry and biology. The former science deals with substances which can be separated from living bodies, and for the chemist specific properties are associated with fixity of substance; but the material with which the biologist is occupied consists of innumerable living unit-individuals exhibiting specific characteristics without fixity of substance. There is no reason to suppose that the properties of a given chemical substance vary in the slightest degree in space or time; but variability and adaptability are characteristic features of all living beings. The biochemist renders inestimable services in elucidating the physico-chemical mechanisms of living organisms; but the problem of individuality and specific behavior, as manifested by living things, is beyond the scope of his science, at least at present. Such problems are essentially of distinctively vital nature and their treatment can not be brought satisfactorily into relation at the present time with the physico-chemical interactions of the substances composing the living body. It may be that this is but a temporary limitation of human knowledge prevailing in a certain historical epoch, and that in the future the chemist will be able to correlate the individuality of living beings with their chemico-physical properties, and so explain to us how living beings first came into existence; how, that is to say, a combination of chemical

substances, each owing its characteristic properties to a definite molecular composition, can produce a living individual in which specific peculiarities are associated with matter in a state of flux. But it is altogether outside the scope and aim of this address to discuss whether the boundary between biochemistry and biology can be bridged over, and if so, in what way. I merely wish to emphasize strongly that if a biologist wishes to deal with a purely biological problem, such as evolution or heredity, for example, in a concrete and objective manner, he must do so in terms of living specific individual units. It is for that reason that I shall speak, not of the chromatin-substance, but of chromatinic elements, particles or units, and I hope that I shall make clear the importance of this distinction.

To return now to our chromatin; I regard the chromatinic elements as being those constituents which are of primary importance in the life and evolution of living organisms mainly for the following reasons: the experimental evidence of the preponderating physiological *rôle* played by the nucleus in the life of the cell; the extraordinary individualization of the chromatin particles seen universally in living organisms, and manifested to a degree which raises the chromatinic units to the rank of living individuals exhibiting specific behavior, rather than that of mere substances responsible for certain chemico-physical reactions in the life of the organism; and last, but by no means least, the permanence and, if I may use the term, the immortality of the chromatinic particles in the life-cycle of organisms generally. I will now deal with these points in order; my arguments relate, in the first instance, to those organisms in which the presence of true cell-nuclei renders the identification of the chromatin-elements certain, as pointed out above, but if the arguments are valid in such cases they are almost certainly applicable also to those simpler types of organisms in which the identification of chromatin rests on a less secure foundation.

The results obtained by physiological experiments with

regard to the functions of the nuclear and cytoplasmic constituents of the cell are now well known and are cited in all the text books. It is not necessary, therefore, that I should discuss them in detail. I content myself with quoting a competent and impartial summary of the results obtained:

> A fragment of a cell deprived of its nucleus may live for a considerable time and manifest the power of coordinated movements without perceptible impairment. Such a mass of protoplasm is, however, devoid of the powers of assimilation, growth, and repair, and sooner or later dies. In other words, those functions that involve destructive metabolism may continue for a time in the absence of the nucleus; those that involve constructive metabolism cease with its removal. There is, therefore, strong reason to believe that the nucleus plays an essential part in the constructive metabolism of the cell, and through this is especially concerned with the formative processes involved in growth and development. For these and many other reasons . . . the nucleus is generally regarded as a controlling centre of cell-activity, and hence a primary factor in growth, development, and the transmission of specific qualities from cell to cell, and so from one generation to another.[20]

I may add here that the results of the study of life-cycles of Protozoa are entirely in harmony with this conception of the relative importance of nuclear—that is chromatinic—and cytoplasmic cell-constituents, since it is not infrequent that in certain phases of the life-cycle, especially in the microgamete-stages, the cytoplasm is reduced, apparently, to the vanishing point, and the body consists solely of chromatin, so far as can be made out. In not one single instance, however, has it been found as yet that any normal stage in the developmental cycle of organisms consists solely of cytoplasm without any particles of chromatin.

While on the subject of physiological experiment, there is one point to which I may refer. Experiments so far have been carried on with Protozoa possessing definite nuclei. It is very desirable that similar experiments should be conducted with forms possessing chromidia in addition to nuclei, in order to test the physiological capa-

[20] E. B. Wilson, "The Cell," second edition, 1911, pp. 30 and 31.

bilities of chromatin-particles not concentrated or organized. *Arcella* would appear to be a very suitable form for such investigations. This is a point to which my attention was drawn by my late friend Mr. C. H. Martin, who has lost his life in his country's service.

I have mentioned already in my introductory remarks that the only reliable test of chromatin is its behavior, and the whole of modern cytological investigation bears witness to the fact that the chromatinic particles exhibit the characteristic property of living things generally, namely, individualization combined with specific behavior. In every cell-generation in the bodies of ordinary animals and plants the chromatin-elements make their appearance in the form of a group of chromosomes, not only constant in number for each species, but often exhibiting such definite characteristics of size and form, that particular, individual chromosomes can be recognized and identified in each group throughout the whole life-cycle. Each chromosome is to be regarded as an aggregate composed of a series of minute chromatinic granules or chromioles, a point which I shall discuss further presently. Most striking examples of the individualization of chromosomes have been made known recently by Dobell and Jameson[21] in Protozoa. Thus in the Coccidian genus *Aggregata* six chromosomes appear at every cell-generation, each differing constantly in length if in the extended form, or in bulk if in the contracted form, so that each of the six chromosomes can be recognized and denoted by one of the letters *a* to *f* at each appearance, *a* being the longest and *f* the shortest.

(*To be continued.*)

[21] *Proc. Roy. Soc.* (B), Vol. 89. (In the press.)